ROCHESTER REGIONAL HEALTH

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CONSENT TO TAKE PART IN A RESEARCH STUDY

Name of Research Study: **Phase 1 Trial to Assess Safety and Tolerability of a Single Dose of *Streptococcus pneumoniae* Whole-Cell Vaccine (wSp) in Healthy Adults**

Address of Research Site: Rochester Clinical Research, 500 Helendale Road, Rochester, NY 14609

Daytime Phone Number: 585-288-0890 24-Hour Phone Number: 585-288-0890

Short Title: STREPTO VAC I

The person in charge of this study is Michael Pichichero, MD., Director of the Rochester General Hospital Research Institute in Rochester NY. The study is overseen and financed by Serum Life Science Europe GmbH, a company based in Germany, acting as the Sponsor.

What is the key information I should know about this study?

This study involves research. Research is not the same as medical care. Research answers scientific questions. These answers can help find new medicines, treatments, vaccines, and even knowledge on how the human body works. This informed consent form tells you about this study. You can ask questions at any time. You can discuss this study with others before deciding to join.

Key things you should know about:

- Taking part in this research study is voluntary (your choice). You do not have to participate, and you can leave the study at any time.
- The purpose of this study is to evaluate the safety and tolerability of a new, unlicensed experimental vaccine against a common bacteria called pneumococcus that causes pneumonia, meningitis and bloodstream infections sinus infections and ear infections in adults and children.
- If you choose to participate, researchers will ask you to agree to visit the research site 4 times. At each visit study personnel will take a brief health history, you will have a physical examination, and at 3 of the visits about 1 tsp of blood will be taken from a vein.
- If your screening medical history, physical examination and blood work prove you qualify for the study at a screening visit (visit 1), then at visit 2 you will receive a vaccination with the experimental vaccine (2 out of 3 chance) or a placebo of salt water (1 out of 3 chance) into a muscle in your arm. The group assignment is random and not known to you or the study team until the study is over.

- You will have access to a 30-day electronic diary to record any reactions or illnesses following the vaccination. You will receive a phone call 3 and 7 days after vaccination to ask you questions about your health and any reactions you have experienced following the vaccination.
- You will be asked to return to the study site for visit 3, which will occur 2 weeks after visit one for an update on your medical history, a physical examination and tests of liver and blood count. Visit 4 will occur 4 weeks after visit one when you will be asked to return to the study site for a final visit for an update on your medical history, a physical examination and tests of liver, blood count, pregnancy test if a female of child-bearing potential, and tests of antibody immunity to the vaccine.
- Possible reactions from the vaccination are redness, tenderness, pain, or swelling at the injection site, and fever, headache and/or fatigue. Some may experience discomfort and/or bruising from the blood draws.
- The vaccine may increase antibody immunity to the pneumococcus bacteria but the possible benefit of such an increase in antibody is unknown.
- The purpose of this study is to determine that the vaccine is safe and tolerated by the adults in this study. The plan is to have the vaccine be tested next in infants.
- The vaccine has been manufactured by two prior vaccine manufacturers (in the USA and in Indonesia) and those vaccines have been tested in adults and toddlers age 1-2 years old. Since then, the manufacturer was changed, and the newly produced vaccine has not been previously tested in adults or children. However, the production technique, release criteria and quality measures for the vaccine are similar and were reviewed for appropriateness by the FDA.

The study staff will give you a signed copy of this form.

The following sections describe the research study in further detail. Please take as much time as you need to ask questions with the study team, with family and friends, or with your personal physician or other healthcare professional. The study team will answer any questions you have before you make a decision.

1. WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to evaluate the safety and tolerability of a novel, unlicensed experimental vaccine against a common bacteria called pneumococcus that causes pneumonia, meningitis and bloodstream infections, sinus infections and ear infections in adults and children. The vaccine to be tested is called Whole-Cell Pneumococcal (wSp) Vaccine.

In the United States, the Centers for Disease Control and Prevention recommend routine pneumococcal vaccination for children younger than 5 years and for adults 50 years or older. The United States currently uses two types of pneumococcal vaccines, conjugate and polysaccharide vaccines. These vaccines presently protect against up to 23 of the 100+ types of pneumococcus bacteria identified. To address the limitations of current pneumococcal vaccines, one approach is to use a whole cell pneumococcal vaccine such as wSp vaccine that may protect against all types of pneumococcus bacteria.

More details about this study can be found on the clinicaltrials.gov website.

2. WHO CAN BE IN THIS STUDY?

Healthy adults aged 18 through 49 years are being recruited and 30 healthy adults will be enrolled in this study.

3. WHAT HAPPENS IF YOU VOLUNTEER FOR THIS STUDY?

If you decide to take part in this study, we will ask you to read and sign this consent document before we do any study-related activities. Next we will screen you to see if you are eligible for this study by asking you questions about your health, performing a physical examination, and drawing blood. If eligible for this study, we will invite you back for an enrollment visit within the next 2 weeks.

At the enrollment visit, we will ask you questions about your health, perform a physical examination, and draw blood for study-related testing. If you are of childbearing potential, we will ask you for urine to perform a pregnancy test. If you still meet eligibility criteria, we will then vaccinate you with a single dose of 1 milligram of wSp vaccine or a placebo of salt water in a volume of 0.5 milliliters (1/10 of a teaspoon) in the muscle of your arm and observe you for 30 minutes. Two-thirds of those enrolled will receive wSp vaccine and one-third will receive the placebo. You will not get to choose which vaccine you receive. The vaccine assignment is random and will not be known to you or the study team until the study is over.

Prior to leaving on the day of study vaccination, you will be trained on how to complete the electronic symptom diary for the first 30 days after vaccination.

If you are a female of child-bearing potential you will be counseled to use an acceptable method of contraception.

Following the enrollment visit (day 1), we will call you on days 3 and 7 and ask you questions about your health and any reactions you have experienced following the vaccination. We will also ask you to come back to the clinic on days 14 and 30 and we will ask you questions about your health, perform a physical examination, and draw blood for study-related testing.

The blood samples taken in this study will be used only for safety monitoring and scientific research. The study team will have access to the samples, which will be stored in a secure place. Each sample will be labeled with a code, and not with your name, so that the lab staff testing the samples will not know your identity. Some of the samples may be used for additional testing related to other studies about vaccines, infections and the bacteria that cause them. The samples will be stored indefinitely after the end of the study and then destroyed when they are no longer useful for research. Your blood samples will not be identifiable to anyone in the research group. A code to match your name and the samples that are taken for the research will be kept by Dr. Pichichero or his designee.

4. WHAT ARE THE RISKS TO BEING IN THIS STUDY?

wSp vaccine has been previously evaluated in clinical studies. One study in the United States included 42 adults and one in Kenya, Africa included 54 adults and 250 toddlers (age 12 to 21 months) with the vaccine made at Walter Reed Army Institute of Research. Additional studies were done in Kenya involving 48 adults and 200 toddlers with the vaccine made by Bio Farma, Indonesia.

In healthy adults in the United States and Kenya, the most common reactions were local pain and tenderness at the injection site, headache, and fatigue. wSp was found to be safe and tolerable. In the Kenyan studies, toddlers experienced injection site redness, tenderness or swelling with some toddlers experiencing fever, irritability, or poor appetite.

Not in adults, but among Kenya toddlers at the same dose as used in this trial, the frequency of vaccinated children experiencing lower respiratory infections was 0% vs. 2% getting the salt water placebo. The frequency of upper respiratory infections was 6% vs. 8% getting placebo and the frequency of upper respiratory infections treated with antibiotics was 4% vs. 8% getting placebo, The testing occurred during the “dry season” when children tend to experience less frequent lower and upper respiratory infections. Among the toddlers in Kenya, Africa that were vaccinated with wSp, more children had upper respiratory infections and received antibiotics than in the placebo group when a lower dose was used than used in this trial. At the lower dose, the frequency of children experiencing lower respiratory infections was 8% vs. 2% placebo. The frequency of upper respiratory infections was 54% vs. 38% getting placebo and the frequency of children with upper respiratory infections being treated with antibiotics was 42% vs.18% getting placebo.

Possible risks from the blood draws include discomfort and/or bruising from the blood draws.

As this is an investigational product and this is the first time the product is being used in humans after the manufacturer has changed, there may be unknown adverse event or serious adverse event/injury that may happen, the likelihood of which we are unaware.

It is important that you tell the study team about all symptoms and side effects if any occur. The phone numbers for the study team are on the first page of this document.

5. WHAT ARE THE BENEFITS OF BEING IN THIS STUDY?

There may be no direct benefit to you to being in this study. You may receive benefit from the wSp vaccination if you are in the vaccination group and not the placebo group. The benefit might be an increase in immunity to pneumococcus bacteria, but it is unknown if any change in the particular immunity raised by this vaccine prevents pneumococcal infections. Information learned from this study may help prevent pneumococcal infections and disease in other adults and children in the future.

6. WHAT IF YOU CHOOSE NOT TO PARTICIPATE IN THIS STUDY?

This study is for research purposes only. You have no obligation to take part in this study. It is voluntary. You can change your mind and drop out of the study later and at any time. There will be no penalty, and you will not lose any benefits you receive now or have a right to receive. Your

medical benefits, rights, and health care will be the same if you decide not to participate in this study or leave the study.

We will tell you if we learn new information that could change your mind about taking part in this study. If you want to drop out, you should tell us. We will make sure you can end the study in the safest way. We will also talk to you about follow-up care, if needed. If you leave the study, your blood samples can be withdrawn at your request if they have not yet been analyzed or destroyed.

The study team or the Sponsor may ask you to leave the study if:

- You do not follow the directions of the study team;
- The study team decides the study is not in your best interest; or
- The study is stopped by the Sponsor, the institutional review board or independent ethics committee (a group of people who review the research to protect your rights), or by a regulatory agency.

7. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF TAKING PART IN THE STUDY?

Injuries sometimes happen in research even when no one is at fault. We will offer you the care needed to treat any injury that results from taking part in this research.

If you think you have been injured or have experienced a medical problem as a result of taking part in this study, contact the Principal Investigator of the study as soon as possible. The Principal Investigator's name and phone number are listed in this consent form.

If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in this study. If possible, you should give them a copy of this informed consent form.

The Sponsor has agreed to pay all reasonable medical expenses for the treatment of reactions, illnesses or injuries related to the use of the study drug, defects in the manufacture of the study drug, or as a direct result of properly performed study tests and/or procedures, except to the extent such expenses are due to the negligence of the study staff or due to your current disease or condition unless it is made worse because you are taking part in this study. The sponsor will cover the reasonable costs of medical treatment for such illnesses and injuries. Any costs for medical care and treatment not paid by the Sponsor will be billed to you or your insurance company. To pay these medical expenses, the Sponsor will need to know some information about you, such as your name, date of birth, and social security number. This is because the clinical study insurance company will check if you have health care insurance and if so, report the payment to the Sponsor. We will not collect your social security number for this purpose unless you are injured, and a claim is submitted to the Sponsor to pay medical expenses.

The Sponsor has not set aside funds to pay for lost wages or any other losses or expenses. However, you are not giving up any of your legal rights by signing this form.

Rochester Regional Health, in fulfilling its public responsibilities, has provided professional liability insurance coverage and will be responsible for any injury in the event such injury is caused by the negligence or professional malpractice of Rochester Regional Health or any of its employees.

8. IS BEING IN THE STUDY VOLUNTARY?

Yes. Taking part in this study is up to you. You may choose not to take part. You can change your mind and withdraw (drop out) later and at any time. There will be no penalty, and you will not lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could change your mind about your taking part in this study. If you want to drop out, you should tell us. We will make sure you can end the study in the safest way. We will also talk to you about follow-up care, if needed.

The study doctor may decide to take you out of the study without your agreement if:

- You do not follow the directions of the study team;
- The study doctor decides that the study is not in your best interest;
- The study is stopped by the Sponsor, the institutional review board (IRB) or independent ethics committee (IEC) (a group of people who review the research to protect your rights), or by a regulatory agency (FDA).

If you withdraw or are removed from the study, blood that have been collected from you that has not yet been analyzed can be destroyed.

9. WHAT WILL I HAVE TO PAY TO TAKE PART IN THIS RESEARCH STUDY?

There will be no charge to you for your participation in this study. The study-related procedures will be provided at no charge to you or your insurance company. However, you and/or your insurer(s) will still be responsible for the costs of your regular medical care.

10. WILL I BE PAID FOR TAKING PART IN THIS STUDY?

For your time and travel expenses related to your participation, you will receive compensation. Based on time for procedures and taking samples and travel expenses the payment will be: Visit 1 (Screening) = $150, Visit 2 (Enrollment and Vaccination) = $200, Visit 3 (Brief History, physical examination and blood test) = $150 and Visit 4 (Brief History, physical examination and blood test) = $150. Phone calls at 3 and 7 days after enrollment and vaccination = $25 each. A single payment will be made for all visits completed.

11. HOW WILL YOUR DATA BE USED AND HOW WILL YOUR PRIVACY AND CONFIDENTIALITY BE PROTECTED WHILE IN THIS STUDY?

Confidentiality of Records and HIPAA Authorization (Data Privacy Statement)
A federal government rule has been issued to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). This rule is designed to protect the confidentiality of your health information. Your health information

is information that could be used to find out who you are. For this study, this includes information in your existing medical records needed for this study and new information created or collected during the study.

This Data Privacy Statement explains how your health information will be used and who it will be given to ("disclosed") for this study. It also describes privacy rights, including your right to see your health information.

By signing the consent document for this study, you will give permission ("authorization") for the uses and disclosures of your health information that are described in this Data Privacy Statement. If you do not want to allow these uses, you should not participate in this study. If you agree to participate in this study, your health information will be used and disclosed in the following ways:

- The study doctor/investigator and study team will use your medical records and information created or collected during this study to conduct the study.
- The study doctor/investigator and study team may send your study-related health information ("study data") anonymously to the US Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), the Sponsor and Sponsor delegated personnel. The study data sent by the study doctor/investigator to FDA, CDC, NIH , the Sponsor and Sponsor delegated personnel will not include your name, address social security number, or other information that directly identifies you, thus it is anonymous. Instead, the study doctor/investigator assigns a numbering code to the study data. Some study data sent by the study doctor/investigator and study team and Sponsor may contain information that could be used (perhaps in combination with other information) to identify you (e.g. date of birth). If you have questions about the specific health information that will be sent, you should ask the study doctor/investigator.
- The study doctor/investigator and study team and Sponsor will use the study data for research purposes to support the scientific objectives described in the consent document and the process of getting regulatory approvals for its vaccines in development and other tests and products.
- The study doctor/investigator and study team and Sponsor may add your study data to data from other studies in research databases to better understand or improve measures of safety and effectiveness, other therapies for patients, or design future clinical studies.
- Your study data, either alone or combined with data from other studies, may be shared with regulatory authorities in the United States and other countries, doctors and scientists at other institutions participating in the study, and the Institutional Review Board overseeing this study.
- Study data that does not directly identify you may be published in medical journals or shared with others as part of scientific discussions.

Your original medical records, which may contain information that directly identifies you, may be reviewed by the Sponsor, the Institutional Review Board overseeing this study, an independent contract research organization that is monitoring the conduct of the study, and regulatory authorities in the United States and other countries. The purpose of these reviews is to assure the quality of the study conduct and the study data, or for other uses authorized by law.

The study doctor/investigator and study team and Sponsor will not disclose personal health information to insurance companies unless required to do so by the law, or unless you provide separate written consent to do so.

Your medical records and study data may be held and processed on computers. No research test results will be included in your medical record.

You have the right to see and copy your personal health information related to this study for as long as this information is held by the study doctor/investigator or their institution. However, to ensure the scientific integrity of this study, you will not be able to review some of the study information until after the study has been completed. When the study is completed, you may request to learn if you received wSp vaccine or placebo and if interested, the results of tests done on samples collected from you. The results will be provided in writing with an explanation of the meaning of the results.

This authorization does not have an expiration date. The study team may need to correct or provide missing information about you even after your study participation is over. Review of your medical records may also take place after the study is over. The study documents will be archived for 2 years after marketing approval or cessation of product development.

You may cancel your authorization at any time by providing written notice to the study doctor/investigator. If you cancel your authorization, the study doctor/investigator and study team will no longer use or disclose your personal health information in connection with this study, unless the study doctor/investigator or study team needs to use or disclose some of your personal health information to preserve the scientific integrity of the study. The study doctor/investigator and Sponsor will still use study data that was collected before you cancelled your authorization. If you cancel your authorization, you will no longer be able to participate in the study. However, if you decide to cancel your authorization and withdraw from the study, you will not be penalized or lose any benefits to which you are otherwise entitled.

12. WHO TO CONTACT WITH QUESTIONS?

Before you sign this document, you should ask questions about anything that you do not understand. The study team will answer your questions before, during, and after the study. If you do not think your question was fully answered or do not understand the answer, please continue to ask until you are satisfied.

If you have any concerns or complaints about this study or how it is being run, please do not hesitate to discuss your concerns with the study team. The phone numbers to reach the study team are on the first page of this document (Daytime Phone Number: **585-288-0890,** 24-Hour Phone Number: **585-288-0890**). If you do not feel comfortable discussing your complaint with the study team, please contact the Institutional Review Board listed below.

If you have any questions about your rights as a study participant, or you would like to obtain information or offer input, or you wish to speak with someone **not** directly involved with the study, you should contact the Institutional Review Board listed below.

IRB Administrator, Rochester General Hospital Investigational Review Board
1425 Portland Avenue, Rochester, NY 14621
Phone: 585-922-5640

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13. SIGNATURES

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I freely consent to take part in this study. I do not give up any of my legal rights by signing this consent document. I understand that I will receive a signed and dated copy of this document.

_____

Printed Name of Study Participant

_____ _____

Signature of Study Participant Date of Signature

Please initial one of the two options below:

_____I agree to the use of my blood for future research.

_____I do **not** agree to the use of my blood for future research.

PERSON OBTAINING CONSENT

_____

Printed Name of the Person Conducting the Consent Discussion

_____ _____

Signature of the Person Conducting the Consent Discussion Date of Signature